Therapy for Secondary Lymphedema

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Description:

TECHNOLOGY AREAS: Biomedical

ACQUISITION PROGRAM: Office of the Principal Assistant for Acquisition

OBJECTIVE: Develop an innovative, curative treatment for secondary lymphedema that will restore the function of the lymphatic vessel system.

DESCRIPTION: Secondary lymphedema is a condition in which blockage or damage to the lymphatic drainage system leads to the retention and build-up of lymphatic fluid in the surrounding tissue. The most common cause of lymphedema in the United States is the surgical removal of part of the lymphatic system in cancer patients, most significantly in breast cancer patients. Chemotherapy and radiation therapy in breast cancer patients can also damage the function of lymph nodes, leading to lymphedema. There are approximately 2.4 million breast cancer survivors in the United States, and each year, about 240,000 women are diagnosed with breast cancer. A recent prospective study found that 42% of breast cancer survivors developed secondary lymphedema within 5 years of their treatment.

Other causes of secondary lymphedema include trauma from burns, surgery, and physical injuries, as well as parasitic infection. Filariasis, a parasitic insect-transmitted infection that is prevalent in tropical regions, is the most common cause of secondary lymphedema internationally. Lymphedema in filariasis infection can progress to a debilitating condition known as elephantiasis.

There is no cure for lymphedema. Quality of life for individuals with lymphedema is diminished. Although lymphedema may be temporary in some cases, chronic lymphedema is an irreversible, debilitating, and lifelong condition that can cause pain and discomfort, disfigurement, skin damage, limb impairments, fibrosis, and recurring risk of infection in the affected tissue. Current treatment options are limited to palliative treatments, including compression sleeves, massage, skin care, bandage wrapping, and exercise.

Recent studies have shown that lymphangiogenesis, or the generation of new lymphatic vessels, can be stimulated by growth factors, such as vascular endothelial growth factor-C (VEGF-C) and angiopoietin-2. Studies combining VEGF-C with other biologics, such as adipose-derived stem cells and autologous lymph nodes, have also demonstrated enhanced lymphangiogenesis compared to VEGF-C alone. The delivery systems tested in these preliminary studies, which were done in animal models, have included novel gel-based systems. Indeed, injectable hydrogel-based systems for drug delivery are a state-of-the-art biomaterials technology, underscoring the potential for developing novel therapies to treat secondary lymphedema.

This topic is seeking to develop and test an innovative curative strategy that will stimulate lymphangiogenesis, resulting in functional lymphatic vessels and restoring lymphatic fluid drainage. An example of a therapeutic strategy would include a combination of molecules or components delivered via an injectable gel, matrix, or other vector that has already demonstrated safety and tolerability in vivo. Administration of the therapeutic will be localized to the affected tissue and will be minimally invasive.

PHASE I: Phase I work will conceptualize the strategy, design the therapeutic system, and test its feasibility. Data obtained in Phase I will provide proof-of-concept that the therapeutic strategy can stimulate lymphangiogenesis using appropriate in vitro cell and tissue culture systems. Assays to test the lymphangiogenic properties of the therapeutic may include lymphatic endothelial cell proliferation, migration, and tube formation and branching. Parameters including optimal concentrations, biological activity, and toxicity will be defined. Appropriate controls will be used. During Phase I, the delivery system will be developed for localized administration in vivo.

PHASE II: Based on Phase I results, Phase II work will demonstrate, optimize and validate the therapeutic strategy in animal models of secondary lymphedema. The FDA approval pathway should be outlined and considered at each developmental stage. Parameters including optimal concentrations, biological activity, and toxicity will be defined. Effectiveness will be determined through histological and/or physiological evidence of lymphangiogenesis and lymphatic flow. Validation of curative success will include the regression or resolution of lymphedema symptoms. During Phase II, clinical experts with insight into relevant patient populations should be consulted during system optimization.

PHASE III: A successful Phase II project will result in a minimally invasive therapeutic modality that restores lymphatic function in secondary lymphedema. During Phase III, additional experiments will be performed as necessary to prepare for FDA review of an IND application. A plan for protection of intellectual property should be created and executed. A detailed market analysis will be conducted, an initial clinical application for the therapeutic will be selected, and a Phase I clinical trial will be initiated. Military application: The therapeutic will be available to service women and men who suffer from lymphedema caused by: treatments for breast or other cancers; burn or other combat- or service-related traumas; and/or infection with filariasis as a result of their deployment in tropical regions. Commercial application: Health professionals worldwide could utilize this therapeutic to treat cancer, trauma, and filariasis patients who suffer from secondary lymphedema.